

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2005/000405

International filing date (day/month/year)
07.02.2005

Priority date (day/month/year)
06.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D417/04, C07D417/14, A61K31/506

Applicant
CYCLACEL LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000405

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000405

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-45
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-45
Industrial applicability (IA)	Yes: Claims	1-45
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Cited Documents

Reference is made to the following documents:

D1: WO 2004/005283

D2: WO 03/029248

D3: WO 01/72745

D4: , ARCHIV DER PHARMAZIE, Med.Chem., **329**, 371-376, (1996)

2. Novelty(Art.33(2)PCT)

The present claims 1-45 relate to thiazole -2- pyrimidine or thiazole-2- pyridine derivatives and pharmaceutical compositions containing them. The prior art documents D1-D4 disclose thiazole -5- pyrimidine derivatives. . The subject matter of the present claims 1-45 can therefore be considered to be novel.

3. Inventive step(Art.33(3)PCT)

3.1 The object of the present application is to provide compounds which are capable of inhibiting one or more protein kinases and are useful for the treatment of diseases and disorders associated with the said kinases.

3.2 In the light of the pharmacological tests comprised in the Description (page 62-66) it is considered as credible that the exemplified compounds have the alleged activity.

3.3 The prior art documents D1- D4 which disclose structurally similar thiazole derivatives having the same pharmacological activity are considered to represent the closest state of the art. With respect to the said prior art documents the main structural difference lies in the attachment position of the thiazole to the pyrimidine/pyridine ring. Taking the above into account it is evident for the person skilled in the art that the further modification of the said attachment position results to more or less potent agents while the protein kinase inhibiting activity is maintained. The claimed compounds are therefore considered to be prima facie obvious and before an inventive step could be acknowledged, it will be necessary for the Applicant to demonstrate that the present compounds display an unexpected property or a particularly advantageous effect compared to the compounds of

the closest state of the art. It has to be stressed that an inventive step could only be based on quantitative data. It should also be taken into consideration that only the structural closest prior art compounds are useful for a meaningful comparison.

3.4 The breadth of the claims should be such that all the compounds comprised should present the said properties and/ or advantages or they will be their obvious modifications. Everything falling within a valid claim has to be inventive otherwise the corresponding claim must be amended accordingly. In this connection it has to be pointed out that the general expressions "hydrocarbyl" "aryl", "alkyl", "cycloheteroalkyl" are non-limitative and are therefore not regarded as obvious modifications or equivalents of the examples which have been given in the description.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-A-2005012298	10. 02. 2005	30. 07.2004	30.07.2003
			05.08.2003
WO-A-2004043953	27.05.2004	14.11.2003	14.11.2002

Re Item VII

Certain defects in the international application

The general expressions "hydrocarbyl" "aryl", "alkyl", "cycloheteroalkyl" contained in the claims are vague and indefinite and as such render the scope of the said claims unclear.

Re Item VIII

Certain observations on the international application

The claims 1 on file contains a disclaimer; the corresponding prior art should be indicated.